Assessment Factors for Toxicity Based Risk Assessment in the Presence of Non-Exchangeable Species

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Outline of presentation:

Assessment Factors

- Assessment Factors (AFs) = Uncertainty Factor; Safety Factor; Extrapolation Factor
- Used to extrapolate species tolerance data $x_1, x_2, \ldots, x_n$ (e.g. LC_{50}s) to multi-species ecosystems **and** address associated uncertainties in order to derive 'safe' concentration levels for regulatory purposes, e.g. pesticide registration, via:

  Safe Conc. $= f(x_1, \ldots, x_n; \text{AF})$

Current Practices & Problem Redefinition

- Current EU practice is deterministic
  $f(x_1, \ldots, x_n; \text{AF}) = \frac{\min\{x_1,\ldots,x_n\}}{AF}$
- It gives a lower concentration which is 'safe' to most species.
  – Doesn't quantify risk!
- **Solution:** use probabilistic modelling which accounts for species tolerance variability and uncertainty to extrapolate to concentration hazardous to p% of the ecological community (HC_p)
- Problem is analogous to estimating p-th percentile of a distribution

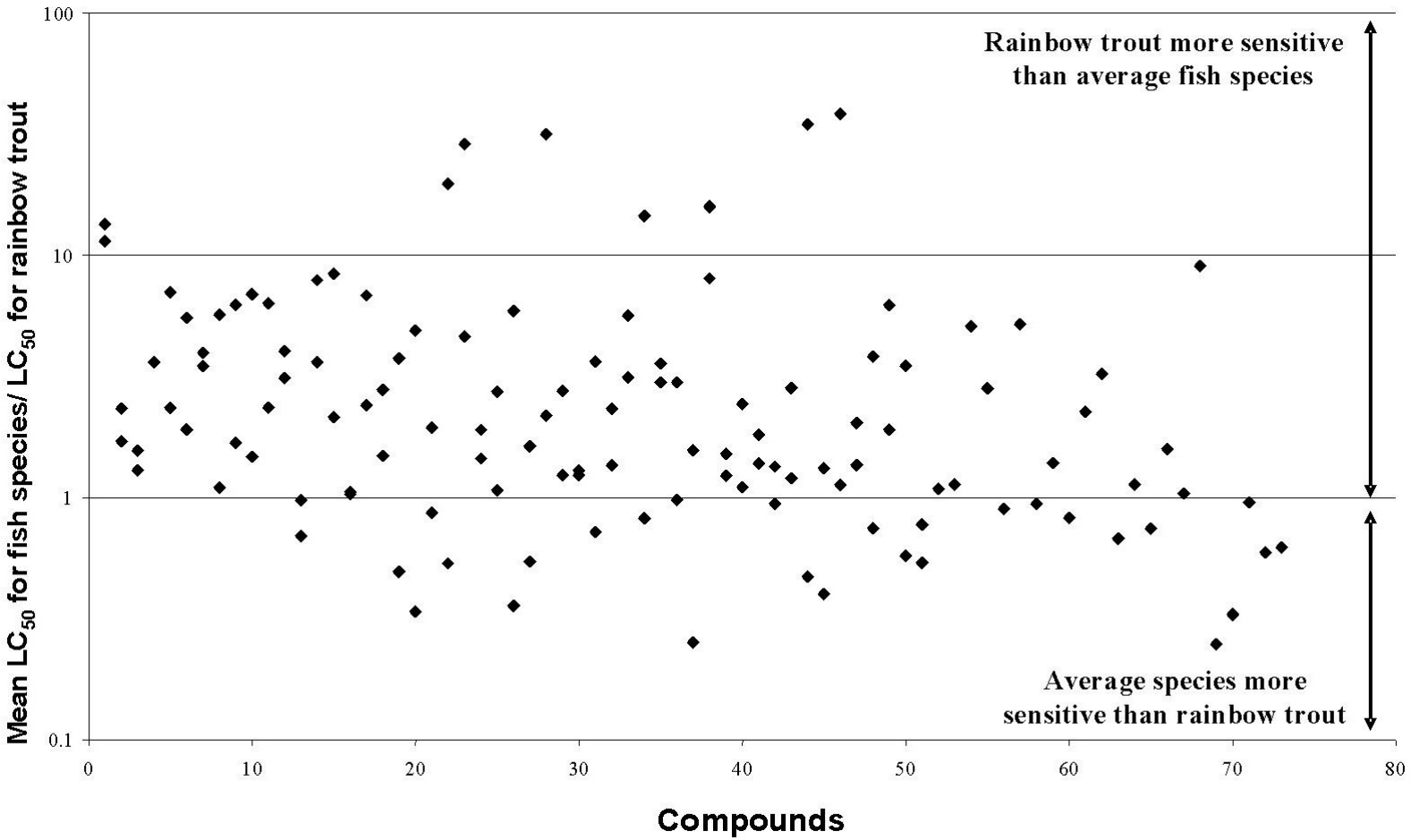
The Species Sensitivity Distribution (SSD)

- A probabilistic model is fitted to the log transformed data $y_1, \ldots, y_n$ – The **SSD**
- Typically assumed $y_1, y_2, \ldots, y_n \overset{iid}{\sim} N(\mu, \sigma^2)$
- If μ and σ^2 known then log-HC$_p = \mu - K_p\sigma$ where $K_p = \Phi^{-1}(1 - p/100)$
- Literature focuses on $p = 5$; driven by Dutch Government
- Decision rules (on log-scale) tend to be of the form $\bar{y} - \kappa_p s$ where κ_p is the Assessment Shift-Factor (ASF)

Species Non-Exchangeability

- SSD assumes all data is *i.i.d.*
- Recent report (EFSA, 2005) noted that the Rainbow Trout may be a *typically* more sensitive species; i.e. tends to lie in the lower half of the SSD
- The Rainbow Trout is a typical dossier species (for logistical reasons)

Background


Rainbow trout more sensitive than average fish species
Average species more sensitive than rainbow trout
Mean LC_{50} for fish species/ LC_{50} for rainbow trout
Compounds
100
10
1
0.1
0
10
20
30
40
50
60
70
80

A Hypothesis Test

- H_0: species i exchangeable; H_1: species i non-exchangeable
- For each species i calculate

$$\hat{R}_i = \sum_{\substack{\text{all substances} \\ \text{in database}}} \text{rank}(species_i)$$

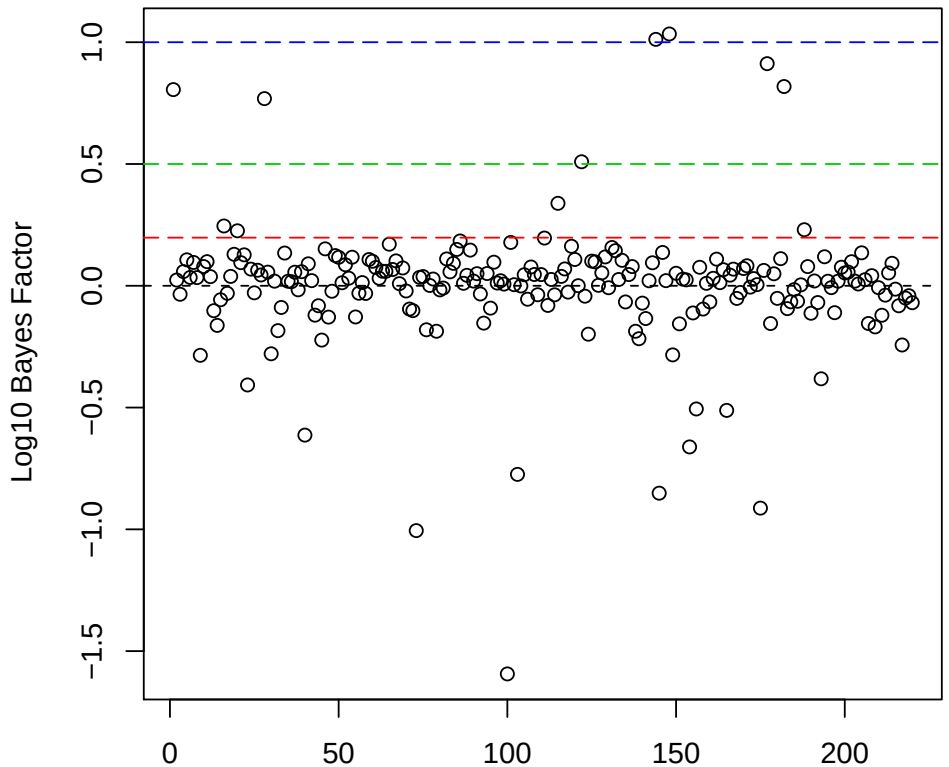
- Generate the true distribution of R_i using Monte Carlo
- Determine a p-value by applying a continuous approximation via the Law of Large Numbers
- Rainbow trout significantly rejected null hypothesis.

Re-Modelling for a Future Risk Assessment (1)

- Let y^* be the special species' log-toxicity value
- Assume $y_i \sim N(\mu, \sigma^2)$ for $i = 1, \ldots, n-1$ and $y^* \sim N(\mu - k, [\phi\sigma]^2)$ (Craig & Hickey, 2008)
- k and ϕ are the **non-exchangeability** parameters – they are properties of the species, not the substance
- We estimate them from a large toxicity database as $\mathcal{MAP}$-estimators, *e.g.* $k_{trout} = 0.195$, $\phi_{trout} = 0.702$

Re-Modelling for a Future Risk Assessment (2)

- An intuitively better model would include:
  $y^* \sim N\left(\mu - k'\sigma, [\phi\sigma]^2\right)$ (EFSA, 2005)
- Costs tractability
- Bayes factor analysis indicates simpler model is not too much worse



NB. Bayes factor is per chemical in the database.

- Apply re-modelled SSD to suitable loss functions: e.g. Generalised Absolute Loss (Aldenberg and Jaworska, 2000); LINEX (Hickey et al., 2008)
- Retrieve optimal p-th percentile estimators of the form:

$$\hat{\mu} - \kappa_p^* \hat{s}$$

where $\hat{\mu}$, $\hat{s^2}$ are found to be new estimators of μ, σ^2; and κ_p^* is a function *independent* of the data and depends on n, p and ϕ.

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The End

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